

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Cinderella BLANCHAT et al. ) Group Art Unit:  
Serial No: ) Examiner:  
Filed: ) Attorney Docket No: 7594-83862  
(SGcsbF1228/2 US)  
For: BIOMATERIAL BASED ON AN )  
INSOLUBILISED DEXTRAN )  
DERIVATIVE AND A GROWTH )  
FACTOR )

**CLEAN VERSION OF ENTIRE SET OF PENDING CLAIMS**

A clean version of the entire set of pending claims is enclosed in accordance with 37 CFR 1.121 (c) (3).

Each claim of the clean version of the entire set of claims begins on a separate page in order to facilitate optical scanning of the claims by the U.S. Patent and Trademark Office.

1. A solid biomaterial, characterized in that it essentially comprises:

(1) at least one solid support material consisting of at least one insolubilized dextran derivative of general formula  $DMC_aB_bSu_cS_d$  in which:

D represents a polysaccharide chain, preferably consisting of successions of glucoside units,

MC represents methyl carboxylate groups,

B represents carboxymethylbenzylamide groups,

Su represents sulfate groups (sulfation of the free hydroxyl functional groups carried by the glucoside units),

S represents sulfonate groups (sulfation of the aromatic rings of the B groups),

a, b, c and d represent the degree of substitution (ds), expressed relative to the number of free hydroxyl functional groups in a glucoside unit of the dextran, respectively in MC, B, Su and S groups; a being  $\geq 0.3$ , b being equal to 0 or  $\geq 0.2$ , c being equal to 0 or  $\geq 0.1$  and d being equal to 0 or  $\leq 0.15$ , provided that when b is equal to 0, c is not equal to 0, and

(2) at least one growth factor exhibiting activity on the osteoarticular, dental and/or maxillofacial tissues.

Year	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	

3. (Amended) The biomaterial as claimed in claim 1, characterized in that said growth factor is selected from the group consisting of EGFs, IGFs, FGFs, TGF- $\beta$ s, PDGFs and BMPs.

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Year	Country	Population (millions)	Urban population (millions)	Urban population (%)	Population density (per sq km)	Urban population density (per sq km)
1970	USA	205	115	56	31	115
1975	USA	220	125	57	33	125
1980	USA	227	132	58	34	132
1985	USA	234	140	60	35	140
1990	USA	242	148	61	36	148
1995	USA	250	155	62	37	155
2000	USA	258	162	63	38	162
2005	USA	266	169	63	39	169
2010	USA	274	176	64	40	176
2015	USA	282	183	65	41	183
2020	USA	290	190	66	42	190
2025	USA	298	197	66	43	197
2030	USA	306	204	67	44	204
2035	USA	314	211	67	45	211
2040	USA	322	218	68	46	218
2045	USA	330	225	68	47	225
2050	USA	338	232	69	48	232
2055	USA	346	239	69	49	239
2060	USA	354	246	70	50	246
2065	USA	362	253	70	51	253
2070	USA	370	260	70	52	260
2075	USA	378	267	71	53	267
2080	USA	386	274	71	54	274
2085	USA	394	281	71	55	281
2090	USA	402	288	72	56	288
2095	USA	410	295	72	57	295
2100	USA	418	302	72	58	302
2105	USA	426	309	73	59	309
2110	USA	434	316	73	60	316
2115	USA	442	323	73	61	323
2120	USA	450	330	73	62	330
2125	USA	458	337	74	63	337
2130	USA	466	344	74	64	344
2135	USA	474	351	74	65	351
2140	USA	482	358	74	66	358
2145	USA	490	365	75	67	365
2150	USA	498	372	75	68	372
2155	USA	506	379	75	69	379
2160	USA	514	386	75	70	386
2165	USA	522	393	75	71	393
2170	USA	530	400	76	72	400
2175	USA	538	407	76	73	407
2180	USA	546	414	76	74	414
2185	USA	554	421	76	75	421
2190	USA	562	428	76	76	428
2195	USA	570	435	76	77	435
2200	USA	578	442	77	78	442

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5. (Amended) The biomaterial as claimed in claim 1, characterized in that it comprises several insolubilized dextran derivatives and/or several growth factors involved in the bone reconstruction process.

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6. (Amended) The biomaterial as claimed in claim 1, characterized in that it is insolubilized by crosslinking with the aid of a crosslinking agent.

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7. The biomaterial as claimed in claim 6, characterized in that said crosslinking agent is selected from the group consisting of sodium trimetaphosphate, epichlorohydrin, divinyl sulfone, gluteraldehyde and bisepoxiranes.

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8. (Amended) The biomaterial as claimed in claim 1, characterized in that it exists in the form of a hydrogel.

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AP

9. (Amended) The biomaterial as claimed in claim 1, characterized in that it exists in the form of a freeze-dried powder.

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AM

10. (Amended) The biomaterial as claimed in claim 9, characterized in that said freeze-dried powder is obtained from biomaterial existing in the form of a hydrogel.

10. (Amended) The biomaterial as claimed in claim 9, characterized in that said freeze-dried powder is obtained from biomaterial existing in the form of a hydrogel.

AD

11. (Amended) The biomaterial as claimed in claim 1, characterized in that it comprises, in addition, a tissue filling material.

11. (Amended) The biomaterial as claimed in claim 1, characterized in that it comprises, in addition, a tissue filling material.

12. The biomaterial as claimed in claim 11, characterized in that it coats particles of an inorganic or polymeric insoluble support, said particles having a diameter greater than 100  $\mu\text{m}$ .

12. The biomaterial as claimed in claim 11, characterized in that it coats particles of an inorganic or polymeric insoluble support, said particles having a diameter greater than 100  $\mu\text{m}$ .

A<sup>a</sup>

13. (Amended) The biomaterial as claimed in claim 11, characterized in that said tissue filling material is selected from the group consisting of collagen, gelatin, biological adhesive, polymers of polylactic or polyglycolic acids, and copolymers of polyethylene glycol and polylactide-co-glycolide.

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[illegible]

15. (Amended) A process for preparing the solid biomaterial as claimed in claim 1, characterized in that the process comprises the following steps:

crosslinking of at least one dextran derivative of general formula  $DMC_aB_bSu_cS_d$  as defined in claim 1 or claim 2,

adsorption, in the insolubilized dextran derivative obtained above, of at least one growth factor as defined in any one of claims 1 to 4,

production of a solid biomaterial according to any one of claims 1 to 8 in the form of a hydrogel,

optionally, the freeze-drying of said hydrogel in order to obtain said biomaterial in the form of a powder.

A12

16. (Amended) The process as claimed in claim 15, characterized in that said crosslinking of at least one dextran derivative of general formula  $DMC_aB_bSu_cS_d$  is carried out with the aid of a crosslinking agent selected from the group consisting of sodium trimetaphosphate, epichlorohydrin, divinyl sulfone, gluteraldehyde and bisepoxiranes.

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17. (Amended) The process as claimed in claim 15, characterized in that the crosslinking of at least one dextran derivative of general formula  $DMC_aB_bSu_cS_d$  is carried out in the presence of a tissue filling material.

17. (Amended) The process as claimed in claim 15, characterized in that the crosslinking of at least one dextran derivative of general formula  $DMC_aB_bSu_cS_d$  is carried out in the presence of a tissue filling material.

Am

18. (Amended) The process as claimed in claim 17, characterized in that said tissue filling material is selected from the group consisting of collagen, gelatin, biological adhesive, polymers of polylactic or polyglycolic acids, copolymers of polyethylene glycol and polylactide-co-glycolide, and an osteoconductive material selected from the group consisting of coral, hydroxyapatite, a mixture of collagen and hydroxyapatite, tricalcic calcium phosphate, calcium sulfate, and calcium carbonate.

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19. (Amended) A process for preparing the biomaterial as claimed in claim 12, characterized in that it comprises the following steps:

bringing the dextran derivative into contact with particles of an inorganic or polymeric insoluble support, as defined in claim 12, so as to obtain a composite,

insolubilization of the composite obtained above, in the presence of a crosslinking agent,

adsorption, in the insolubilized composite obtained above, of at least one of said growth factors.

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Year	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	

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22. (Amended) The use of a solid biomaterial as claimed in claim 1 for the preparation of a coating for orthopedic, dental or maxillofacial prostheses.

22. (Amended) The use of a solid biomaterial as claimed in claim 1 for the preparation of a coating for orthopedic, dental or maxillofacial prostheses.

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